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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/580,237	05/23/2006	Christopher Penney	GRT/4141-20	1942

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EXAMINER	
BALASUBRAMANIAN, VENKATARAMAN	
ART UNIT	PAPER NUMBER
1624	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/580,237	PENNEY ET AL.	
	Examiner	Art Unit	
	/Venkataraman Balasubramanian/	1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 May 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-24* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-24* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *5/23/2006*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The preliminary amendment, which included amendment to claims 4, 6-9 and 21-24, filed on 5/23/2006, is made of record. Claims 1-24 are pending.

Information Disclosure Statement

References cited in the Information Disclosure Statement, filed on 5/23/2006, are made of record.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-24 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

1. Recitation of "aminyl" group and "diaminyl" group in claims 18 and 25-29, renders these claims and their dependent claims indefinite as it is not clear what these groups are. In addition, if they were meant to be amino and diamino group as it appears to be in claim 21, then these claims lack consistency in the definition of variables.

In addition, it is also not clear what is meant by "multivalent aminyl group" and "diaminyl group terminated spacer. It is not clear whether X links both triazine through nitrogen or other group.

2. In claim 21 is again vague and unclear as to the choice of X as diaminoalkane. It is no clear whether the link between two triazines is through nitrogens or not. Similarly, whether is M linked to the rest of the molecule through nitrogen or not is unclear.

3. Claim 22 is indefinite as it is not clear what "each" is referred to. In addition the choice of secondary and primary appears to be monovalent and hence it is not clear where they are to be appended.

4. Claim 23 appears to be improper dependent claim as claim 18 never indicates carboxy substituents.

5. Independent claim 24 is indefinite as it lacks variable group definitions.

6. Claim 5 is indefinite as it is not clear how X is appended to M if M were a amine-containing matrix and x itself is aminyl or diaminyl terminated with a spacer.

7. Claim 26 is in definite as it is cryptic and confusing. It recites steps, which were not recited in claim 25 on which claim 26 is dependent.

8. Claim 27 is indefinite as it recites related compounds. It is not clear what is meant by related compounds.

9. Claim 28 is indefinite as it recites related compounds and cryptic as to the process recited therein. It is not clear what is meant by related compounds. In addition, it is not clear what intermediates are synthesized and how. What are the appropriate steps for conversion of these structures?

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 29-33 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for isolation of monoclonal antibodies by affinity

chromatography, does not reasonably provide enablement for separation, isolation, purification, characterization, identification of any or all entities, quantification or discovery of peptides and proteins and including toxic or pathogenic entities from a biological or pharmaceutical compound as generically embraced in the claim language. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims. Following apply.

In evaluating the enablement question, several factors are to be considered. Note *In re Wands*, 8 USPQ2d 1400 and *Ex parte Forman*, 230 USPQ 546. The factors include: 1) The nature of the invention, 2) the state of the prior art, 3) the predictability or lack thereof in the art, 4) the amount of direction or guidance present, 5) the presence or absence of working examples, 6) the breadth of the claims, and 7) the quantity of experimentation needed.

1. **The nature of the invention and the state of the prior art:**

The instant method of use claims 29-33, are drawn to a method of separation, isolation, purification, characterization, identification, quantification or discovery of peptides and proteins, or for the removal of contaminants, including toxic or pathogenic entities, from a preparation of biological or pharmaceutical compound in general.

Instant claims, as recited, are reach through claims. A reach through claim is a claim drawn to a mechanistic, receptor binding or enzymatic functionality in general format and thereby reach through a scope of invention for which they lack adequate written description and enabling disclosure in the specification.

In the instant case, based on the affinity of the instant compounds toward proteins, instant claims reaches through to a method of separation, isolation, purification, characterization, identification of any or all entities, quantification or discovery of peptides and proteins, or for the removal of any or all contaminants, including toxic or pathogenic entities, from a preparation of biological or pharmaceutical compound in general and thereby they lack adequate written description and enabling disclosure in the specification.

More specifically, in the instant case, based on the mode of action of instant compounds as affinity ligands, based on limited assay, it is claimed that method of separation, isolation, purification, characterization, identification of any or all entities, quantification or discovery of peptides and proteins, or for the removal of any or all contaminants, including toxic or pathogenic entities, from a preparation of biological or pharmaceutical compound in general, which there is no enabling disclosure.

Specification is not adequately enabled for the all the above said method of uses of compounds of formula (I). Specification has one example of isolation of monoclonal antibodies and screening for protein binding to affinity material comprising instant compounds (pages 17-19). However, there is no enabling of such compounds in all the above said uses. For example, it is not clear how would one characterize and identify any entities merely based on the fact the instant compounds show affinity for protein binding. Such a process requires much more sophisticated methodologies than simple affinity chromatography. Likewise separation different entities require more than binding and releasing all bound proteinaceous material as embraced in the instant claims.

The compound of formula I embrace bis-triazine compounds substituted with variable groups, X, Y and Z.

Even a cursory calculation of the number of compounds embraced in the instant formula (I) based on the generic definition of aminyl, multivalent aminyl, diaminyl and support matrix M etc would result in very large genus of compounds. Thus the genus embraced in the claim 1 is too large and there is no teaching of for all the method of uses of this large genus.

In addition, even with proteins, it is not usually possible to predict which protein will bind to which matrix with which affinity ligand. Thus, in the absence of any guidance in the specification and without extensive experimentation one cannot predict if a particular ligand with a particular matrix will bind a particular protein. This is quite evident from the screening protocol used in the instant specification.

2. **The predictability or lack thereof in the art:**

Hence, the method of uses for separation, isolation, purification, characterization, identification of any or all entities, quantification or discovery of peptides and proteins and including toxic or pathogenic entities from a biological or pharmaceutical compound embraced in the instant claims are not art-recognized methods of uses and hence there should be adequate enabling disclosure in the specification with working example(s).

Note substantiation of utility and its scope is required when utility is "speculative", "sufficiently unusual" or not provided. See Ex parte Jovanovics, 211 USPQ 907, 909; In re Langer 183 USPQ 288.

Next, applicant's attention is drawn to the Revised Utility and Written Description Guidelines, at 64 FR 71427 and 71440, wherein it is emphasized that 'a claimed invention must have a specific and substantial utility'. The disclosure in the instant case is not sufficient to enable the instantly claimed method treating solely based on the inhibitory activity disclosed for the compounds. The state of the art is indicative of the requirement for undue experimentation.

3. **The amount of direction or guidance present:**

Example 8 illustrated in the experimental section are limited to isolation of monoclonal antibodies. There are no examples of separation, isolation, purification, characterization, identification of any or all entities, quantification or discovery of peptides and proteins and including toxic or pathogenic entities from a biological or pharmaceutical compound. Even with proteins, based on the screening assays, it is clear that merely bring the any of the instant compound with any protein does not result in binding and isolation. Additional direction or guidance is needed to make the method viable for any or all entities. Specication has no such direction or guidance.

4. **The presence or absence of working examples:**

There is no working example of for separation, isolation, purification, characterization, identification of any or all entities, quantification or discovery of peptides and proteins and including toxic or pathogenic entities from a biological or pharmaceutical compound. These methods cannot be simply willed into existence. As was stated in Morton International Inc. v. Cardinal Chemical Co., 28 USPQ2d 1190 "The specification purports to teach, with over fifty examples, the preparation of the claimed

compounds with the required connectivity. However ... there, is no evidence that such compounds exist... the examples of the '881 patent do not produce the postulated compounds... there is ...' no evidence that such compounds even exist." The same circumstance appears to be true here. There is no evidence that separation, isolation, purification, characterization, identification of any or all entities, quantification or discovery of peptides and proteins and including toxic or pathogenic entities from a biological or pharmaceutical compound is feasible by single class of affinity ligands and support matrix..

5. **The breadth of the claims & the quantity of experimentation needed:**

Specication has no support, as noted above, for compounds generically embraced in the claims 1-8 would lead to desired method of separation, isolation, purification, characterization, identification of any or all entities, quantification or discovery of peptides and proteins and including toxic or pathogenic entities from a biological or pharmaceutical compound.. As noted above, the genus embraces large number of compounds and support matrix and hence the breadth of the claim is broad. The quantity of experimentation needed would be an undue burden on skilled art in the chemical art since there is inadequate guidance given to the skilled artisan for the many reasons stated above. Even with the undue burden of experimentation, there is no guarantee that one would get the desired method of separation, isolation, purification, characterization, identification of any or all entities, quantification or discovery of peptides and proteins and including toxic or pathogenic entities from a biological or pharmaceutical compound embraced in the instant claims .

Also, note MPEP 2164.08(b) which states that claims that read on "... significant numbers of inoperative embodiments would render claims nonenabled when the specification does not clearly identify the operative embodiments and undue experimentation is involved in determining those that are operative.". Clearly that is the case here.

MPEP 2164.01(a) states, "A conclusion of lack of enablement means that, based on the evidence regarding each of the above factors, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation. In re Wright, 999 F.2d 1557,1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993)." That conclusion is clearly justified here. Thus, undue experimentation will be required to make Applicants' invention.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 18-22 and 24-33 are rejected under 35 U.S.C. 102(b) as being anticipated by Lowik et al., WO 01/42228.

Lowik et al., teaches several triazines compounds and their use as affinity ligands on solid supports. See pages 1-3 for description of the invention and Schemes 1-8 for various triazines made and attached to solid support. See pages 4-8 for

examples 1-5 and pages 8-19 for compounds 1-53b. Especially see example 2 and various examples in Schemes (Figures 3a, 3b, 6 and 7).

Claims 18-20 and 24-33 are rejected under 35 U.S.C. 102(b) as being anticipated by Atkinson et al., GB 2053 926.

Atkinson et al., teaches various triazine compounds useful as affinity chromatography materials attached to a solid support. See page 1-2, especially page 2, lines 40-45. See table 1, Note Procion Red HE-3b is taught as ligand for attachment to solid support.

Claims 18-20 and 24-28 are rejected under 35 U.S.C. 102(b) as being anticipated by Dore et al., GB 2 149 808.

Dore et al., teaches various triazine compounds useful as dyes for dyeing various materials. See entire document especially see example 61 and 91b.

Claims 18-20 and 24-28 are rejected under 35 U.S.C. 102(b) as being anticipated by Adam et al., EP 0 122 458.

Adam et al., teaches various triazine compounds useful as dyes for dyeing various materials. See entire document especially see examples 72-93.

Claims 18-22 and 24-28 are rejected under 35 U.S.C. 102(b) as being anticipated by Cipolli et al., EP 0 542 374.

Cipolli et al., teaches various triazine compounds useful for incorporating into various materials. See entire document especially Table 1, examples 1-24.

Claims 18-22 and 24-28 are rejected under 35 U.S.C. 102(b) as being anticipated by Lawery et al., US 6,482,255.

Lawery et al., teaches various triazine compounds useful for ink-jet printing. See entire document especially examples 1-27.

Claims 18-22 and 24-28 are rejected under 35 U.S.C. 102(b) as being anticipated by Karrer et al., US 4,731,393.

Karrer et al., teaches various triazine compounds and their bonding to polymer . See entire document especially examples 1-6 for triazine compounds and examples A-E for bonding of these compounds to polymer.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation

under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-22 and 24-33 are rejected under 35 U.S.C. 103(a) as being unpatentable over Dore et al., GB 2 149 808 or Adam et al., EP 0 122 458 or Cipolli et al., EP 0 542 374 or Lawery et al., US 6,482,255 or Karrer et al., US 4,731,393 in view of Lowik et al., WO 01/42228 and Atkinson et al., GB 2053 926.

Teachings of Dore et al., Adam et al., Cipolli et al., Lawery et al.,, Karrer et al., and Atkinson et al., as discussed in the above 102 rejections are incorporated herein. As noted above, Dore et al., Adam et al., Cipolli et al., Lawery et al., and Karrer et al., teach several triazines compounds and their attachment to various support materials. But they did not teach the use of these triazines for affinity chromatography of proteinaceous materials.

The secondary reference, Lowik et al., teaches several triazines bound matrix for affinity chromatography and Atkinson et al., teaches use of several triazines in affinity chromatography. These two references teaches equivalency of the various triazines and their bound form for affinity chromatography. Thus, it would be obvious to one trained in the art to use polymer bound triazine compounds for affinity chromatography of proteins in view of the equivalency teaching outlined above. See In re KSR International vs Teleflex Inc., 82 USPQ2d 13-85, 1397 (2007).

Conclusion

Any inquiry concerning this communication from the examiner should be addressed to Venkataraman Balasubramanian (Bala) whose telephone number is (571) 272-0662. The examiner can normally be reached on Monday through Thursday from 8.00 AM to 6.00 PM. The Supervisory Patent Examiner (SPE) of the art unit 1624 is James O. Wilson, whose telephone number is 571-272-0661. The fax phone number for the organization where this application or proceeding is assigned (571) 273-8300. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAG. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-2 17-9197 (toll-free).

Venkataraman Balasubramanian

8/9/2007